

WHAT IS CLAIMED IS:

1. A method for pulsatile systemic delivery of an active fragment of parathyroid hormone (PTH) to a mammalian host, said method comprising:

inhalation through the mouth by the host of a dispersion of an N-terminal fragment of PTH having a length which results in a pulsatile serum profile characterized by a rapid rise followed by a rapid fall after a peak has been released.

2. A method as in claim 1, wherein the PTH fragment has 50 or fewer amino acids.

3. A method as in claim 1, wherein the PTH is a fragment consisting essentially of amino acids 1-34 or 1-38 of Table 1.

4. A method as in claim 1, wherein the total dosage of PTH fragment is in the range from 100  $\mu$ g to 2,000  $\mu$ g per day, resulting in systemic availability in the range from 50 $\mu$ g to 500  $\mu$ g per day.

5. A method as in claim 1, wherein the PTH fragment dispersion comprises a dry powder including a bulking agent.

6. A method as in claim 1, wherein the PTH fragment dispersion comprises a nebulized liquid solution or suspension of the PTH fragment.

7. A method as in claim 1, wherein the PTH fragment dispersion comprises a dry powder and an aerosol propellant.

8. A method as in claim 1, further comprising administering vitamin D or dietary calcium to the host in order to treat osteoporosis.

9. A method for pulsatile systemic delivery of an active fragment of parathyroid hormone (PTH) to a patient, said method comprising:

(a) dispersing a preselected amount of the PTH fragment in a volume of gas to produce an aerosolized bolus;

(b) inhaling of the aerosolized bolus by the patient through the mouth and into the alveolar region of the lungs; and

repeating steps (a) and (b) a sufficient number of times until a desired total dosage of PTH fragment is delivered.

10. A method as in claim 9, wherein the PTH is a fragment consisting essentially of amino acids 1-34 or 1-38 of Table 1.

11. A method as in claim 9, wherein the aerosolized bolus contains from about 50  $\mu\text{g}$  to 500  $\mu\text{g}$  of PTH fragment and the total dosage is from about 100  $\mu\text{g}$  to 2,000  $\mu\text{g}$  per day, resulting in systemic availability in the range from 50  $\mu\text{g}$  to 500  $\mu\text{g}$  per day.

12. A method as in claim 9, wherein the aerosolized bolus has a volume in the range from 10 ml to 750 ml.

13. A method as in claim 9, wherein the PTH fragment is dispersed in an aerosol of particles in the size range from 0.5  $\mu\text{m}$  to 5  $\mu\text{m}$ .

14. A method as in claim 9, wherein the PTH fragment comprises a dry powder present in a bulking

agent, and dispersing comprises introducing the dry powder into a high velocity gas stream.

5 15. A method as in claim 9, wherein the PTH fragment comprises a liquid solution or suspension, and dispersing comprises nebulization of the liquid.

10 16. A method as in claim 9, wherein the PTH fragment comprises a liquid or powder present in a propellant, and dispersing comprises releasing the propellant through a nozzle to produce the dispersion.

15 17. A method as in claim 9, further comprising administering vitamin D or dietary calcium to the patient in order to treat osteoporosis.

20 18. A pharmaceutical composition comprising a biologically active N-terminal fragment of parathyroid hormone (PTH) present as a dry powder having a mean particulate size in the range from 0.5  $\mu\text{m}$  to 5  $\mu\text{m}$ ; and a pharmaceutically acceptable dry bulking powder, wherein the PTH is present at from 1% to 25% by weight.

25 19. A pharmaceutical composition as in claim 18, wherein the bulking powder is composed of a material selected from the group consisting of sucrose, lactose, trehalose, HSA, glycine, cellobiose, dextran, maltotriose, pectin, sodium citrate, sodium ascorbate, and mannitol.

30 20. A pharmaceutical composition comprising a biologically active N-terminal fragment of parathyroid hormone (PTH) present as a powder having a mean particle size in the range from 0.5  $\mu\text{m}$  to 5  $\mu\text{m}$  present in an aerosol propellant.

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21. A pharmaceutical composition as in claim 20, wherein the aerosol propellant is a chlorofluorocarbon or a hydrofluorocarbon.

5           22. A pharmaceutical composition suitable for nebulization, said composition comprising a biologically active fragment of parathyroid hormone present in an aqueous buffer at pH 4-6 and a concentration in the range from 1 mg/ml to 20 mg/ml.

10           23. A pharmaceutical composition as in claim 22, wherein the buffer is selected from the group consisting of acetate, ascorbate, and citrate, each at 5 mM to 50 mM.

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